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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,565	08/11/2005	Ian Alexander Shiels	36672.9	1391

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EXAMINER	
ZAREK, PAUL E	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
11/21/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/531,565	SHIELS ET AL.	
	Examiner	Art Unit	
	Paul Zarek	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *2-5,21 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6-20,22 and 24-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 April 2008* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/24/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claim 26-28 were added in correspondence filed on 10/08/2008. Claims 1-28 are currently pending. This is the first Office Action on the merits of the claim(s).

Election/Restrictions

2. Applicant's election without traverse of AcF[OPdChaWR], also known as PMX53 (inhibitor of a GPCR), infliximab (second agent), and dermatitis (hypersensitivity condition) in the reply filed on 10/08/2008 is acknowledged. Claims 1, 6-20, 22, and 24-28 read on the elected species. Claims 2-5, 21, and 23 are withdrawn as being drawn to a nonelected species.

Priority

3. Applicant's claim for the benefit of a prior-filed international application PCT/AU03/01374 (filed on 10/16/2003 under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. The effective filing date of the instant application is 10/16/2003.

4. Acknowledgment is made of applicant's claim for foreign priority based on an application 2002952129 filed in Australia on 10/17/2002. The priority date of the instant application is 10/17/2002.

Double Patenting

5. Applicant is advised that should Claim 15 be found allowable, Claim 25 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112 (1st paragraph)

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 6-20, 22, and 24-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating a hypersensitivity condition comprising administration of a composition comprising formula I, does not reasonably provide enablement for prevention of a hypersensitivity condition comprising administration of a composition comprising formula I. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

8. *In re Wands*, 858 F.2d at 736-40, 8 USPQ2d at 1403-07, set forth eight factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." (MPEP § 2164.01(a))

a. *The breadth of the claim*: Claims 1, 6-20, 22, and 24-28 are drawn to a method of treatment of a hypersensitivity condition. The instant specification defines "treatment" to include preventing the disease from occurring, inhibiting the disease, or ameliorating the effects of the disease.

"Prevent" and "prevention" are potent words implying that the method of prevention will necessarily prevent a hypersensitivity condition in a subject at any point following administration of formula I. Accordingly, if a subject suffers from even one hypersensitivity condition at some point following administration of formula I, then the method is no longer considered to be a prevention method;

b. *Nature of the invention*: The nature of the invention is a method of treating, but not preventing, a hypersensitivity condition in a subject comprising the administration of a composition comprising formula I;

c. *The state of the prior art*: The prior art demonstrates that AcF[OPdChaWR] (PMX53), a species of formula I is an effective C5a receptor antagonist that suppresses pro-inflammatory cytokines, such as TNF-α and IL-6 (Strachen, et al., Journal of Immunology, 2000, abstract). Hypersensitivity conditions, such as dermatitis, are modulated by C5a and the C5aR on eosinophils (Czech, et al., Scandinavian Journal of Immunology, 2001, Introduction). C5aR antagonists are effective treatments for hypersensitivity conditions, such as dermatitis.

The inflammatory milieu is a complex and dynamic microenvironment in which the ultimate outcome of the inflammatory response is dependent upon the balance of pro- and anti-inflammatory signals (i.e. cytokines) that are present. The presence, or even

relative abundance of any one signal would not necessarily tip the balance from a pro-inflammatory response (i.e. dermatitis) to a non-inflammatory response;

d. *Level of one of ordinary skill in the art*: Dermatologists and scientists investigating the skin and diseases of the skin would comprise an ordinarily skilled artisan. As such, the level of ordinary skill would be high;

e. *Level of predictability in the art*: Cyclic peptides of formula I are known to be antagonists of the C5aR. C5aR antagonists are effective treatments for hypersensitivity conditions. Examiner found no reports indicating that C5aR antagonists can prevent hypersensitivity conditions;

f. *Amount of direction provided by the inventor and existence of working examples*: Applicant provides examples of formula I (usually PMX53) as a therapy for hypersensitivity conditions, such as Arthus reactions (Type III hypersensitivity conditioin), asthma, and allergic dermatitis. All *in vivo* examples utilize treatment models, not prevention models; and,

g. *Quantity or experimentation needed to make or use the invention based on the content of the disclosure*: To use the invention as claimed, one of ordinary skill in the art would have to identify who would suffer from hypersensitivity conditions in the future and provide a therapy in advance of the onset of the actual hypersensitivity condition. After identifying who was about to suffer hypersensitivity condition, the skilled artisan would then need to determine the cause of the hypersensitivity condition and administer enough of formula I to shift the immune response from pro-inflammatory to a non-inflammatory response. Given the complexity of the microenvironment, it is unclear

what the effective dose of formula I would be, and whether it would be different depending upon the type of hypersensitivity condition (i.e. dermatitis versus asthma). The instant specification provides no guidance for a skilled artisan to identify a subject about to experience a hypersensitivity condition, nor does it provide information as to a dose or administration schedule of formula I to prevent said condition. The art does not make up for this deficiency. The instant specification and art would not enable one of ordinary skill in the art to use the invention commensurate with the scope of the rejected claims. Undue and unpredictable experimentation would be required. Limiting the invention to a method of treatment, inhibition or amelioration of hypersensitivity conditions, but not preventing said conditions, would overcome this rejection.

11. Claims 13 and 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 13 and 14 are drawn to a method of treating hypersensitivity conditions wherein the compound is described in PCT/AU02/01427. The instant specification does not specifically disclose compounds 1-6, 10-15, 17, 19, 20, 22, 25, 26, 28, 30, 31, 33, 37, 39-45, 47-50, 52-58, and 60-70, but references the international application. As these compounds are distinctly claimed, they are considered "essential material" to the instant disclosure. 'Essential material' may be incorporated by reference, but only by way of an incorporation by reference to a U.S. patent or a U.S. patent application publication, which patent or patent application does not itself incorporate such

essential material by reference." (37 CFR § 1.57(c)) Essential material is necessary for the written description of the claimed invention. Since compounds 1-6, 10-15, 17, 19, 20, 22, 25, 26, 28, 30, 31, 33, 37, 39-45, 47-50, 52-58, and 60-70 are not particularly described in the instant disclosure, and are not incorporated by reference to a US patent or patent application publication, Claims 13 and 14 are not considered to be enabled by the instant specification. Amending the specification to particularly include compounds 1-6, 10-15, 17, 19, 20, 22, 25, 26, 28, 30, 31, 33, 37, 39-45, 47-50, 52-58, and 60-70 would overcome this rejection.

Claim Rejections - 35 USC § 112 (2nd paragraph)

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 13 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: compounds 1-6, 10-15, 17, 19, 20, 22, 25, 26, 28, 30, 31, 33, 37, 39-45, 47-50, 52-58, and 60-70. The instant specification does not distinctly disclose the claimed compounds, but incorporates an international application by reference. The claimed compounds are considered essential material to the instant application and essential material can only be incorporated by reference from US patents or US patent applications (37 CFR § 1.57(c)(2)).

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 1, 6-14, 17-20, 26, and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Strachan, et al. (above), in view of Czech, et al. (above).

17. Claims 1 and 26 of the instant application is drawn to a method of treating a hypersensitivity condition (of which dermatitis is the elected species) comprising administration of a composition comprising formula I (of which PMX53 or compound 1 is the elected species) or PMX53, respectively. Claims 6-9 limit the subgroups B, C, D, and E, respectively. PMX53, the elected species, reads on Claims 6-9. Claims 10-12 limit the compound of formula I to possess C5aR antagonist activity but no C5aR agonist activity (Claim 10), be an inhibitor at sub-micromolar concentrations (Claim 11) and have a receptor affinity and antagonist potency with IC_{50}s of <25 μM and 1 μM, respectively (Claim 12). Claims 12 and 13 claim specific

compounds, including compound 1, the elected species. Claim 17 limits the treatment to acute recurrence of a hypersensitivity condition. Claim 18 limits the treatment to treat the primary occurrence of a hypersensitivity condition. Claims 19, 20, and 28 limit the hypersensitivity conditions to be treated.

18. Strachan, et al., teach that the elected compound (termed AcF[OPdChaWR] in this art) is a C5aR antagonist and is a potent anti-inflammatory agent, able to suppress pro-inflammatory cytokines such as TNF-α and IL-6 (pg 6560, col 2, paragraph 1). AcF[OPdChaWR] was an effective treatment for the arthus reaction, which is a model of Type III hypersensitivity. Strachan, et al., does not discuss the properties of AcF[OPdChaWR], or the use of AcF[OPdChaWR] to treat dermatitis.

19. Since Strachan, et al., teaches the claimed compound, it inherently meets all the functional limitations to said compound of Claims 6-12.

20. Czech, et al., teach that eosinophils play an important role in atopic dermatitis. C5a binds to the C5a receptor on the eosinophils to activate the eosinophils and induce dermatitis (pg 235, col 2, paragraph 1). Since C5a activates eosinophils to induce dermatitis and the elected species is known to be a C5aR antagonist, anti-inflammatory, and an effective therapy for the arthus reaction, it would have been *prima facie* obvious to one of ordinary skill in the art to use the elected species for the treatment of dermatitis.

21. Claims 15, 16, and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Strachan, et al., and Czech, et al., as applied to claim1, 6-14, 17-20, 25, 26, and 28 above, and further in view of Laduca and Gaspari (Dermatologic Clinics, 2001).

22. Claims 15, 16, and 27 of the instant application are drawn to a method of treating a hypersensitivity condition (of which dermatitis is the elected species) comprising administration of a composition comprising formula I (of which PMX53 or compound 1 is the elected species) or PMX53 (Claim 27), further comprising a second agent (of which infliximab is the elected species).

23. Strachan, et al., and Czech, et al., teach a treatment for dermatitis comprising the elected compound. Strachan, et al., and Czech, et al., do not teach the addition of infliximab.

24. Laduca and Gaspari teach that TNF-α is the prominent cytokine that is important in contact dermatitis and that infliximab would be efficacious for inflammatory skin conditions, such as dermatitis (abstract). "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (MPEP § 2144.06(I). Therefore, it would have been *prime facie* obvious to one of ordinary sill in the art to combine the PMX53 and infliximab for the treatment of dermatitis.

25. Claims 22 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Strachan, et al., and Czech, et al., as applied to claims 1, 6-14, 17-20, 25, 26, and 28 above, and further in view of Fairlie, et al. (International Application No. WO 99/00406, provided in IDS).

26. Claims 22 and 24 of the instant application further limit the method of Claim 1 to specific administration routes, including oral.

27. Strachan, et al., and Czech, et al., teach a treatment for dermatitis comprising the elected compound. Strachan, et al., and Czech, et al., do not teach an oral formulation of the elected species.

28. Fairlie, et al., teach the same cyclic polypeptide of formula I and teach that oral administration is the preferred route of administration due to its greater convenience and acceptability (pg 19, lines 28-30). Therefore, it would have been *prima facie* obvious to make PMX53 into an oral formulation for the treatment of dermatitis.

Conclusion

29. No claims are allowed.

30. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul Zarek whose telephone number is (571) 270-5754. The examiner can normally be reached on Monday-Thursday, 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

PEZ

/Rita J. Desai/
Primary Examiner, Art Unit 1625